[1]Adelphi Real World, Bollington, Cheshire, UK, [2]Tolley Health Economics, Buxton, UK, [3]Allergan, LLC, Irvine, CA, USA, [4]Adelphi Real World, Macclesfield, Cheshire, UK

BACKGROUND: Disease-specific instruments, commonly incorporated into clinical trials, provide comprehensive insights into the quality-of-life of patients experiencing that disease. However it is not possible to directly elicit preference-based valuations from such instruments for use in cost-utility analysis. **OBJECTIVES:** To provide a mapping algorithm for estimating EQ-5D index scores from the Urinary Incontinence-specific Quality of Life Questionnaire (I-QOL) based on nationally representative samples of patients with idiopathic or neurogenic overactive bladder (OAB) syndrome using EQ-5D preference valuations based on both the UK and US general populations. **METHODS:** Analyses were conducted for 2505 patients from the Adelphi OAB Disease Specific Programme, a cross-sectional study of patients consulting with idiopathic or neurogenic OAB, undertaken in the USA and Europe in 2010. A range of statistical mapping techniques including OLS, CLAD, Tobit, GLMs, reverse GLMs and reverse two-part GLMs were used. Ten-fold cross validation techniques were employed to calculate Mean Absolute Error (MAE) and Root Mean Squared Error (RMSE) goodness of fit statistics. Various predictor lists together with a method combining stepwise selection with multivariable fractional polynomial techniques to allow non-linear relationships to feature were pursued. **RESULTS:** Choice of predictors was consistent for both the UK and USA EQ-5D tariffs. For idiopathic, the best model included IQOL Composite Score and age (both modelled non-linearly). For neurogenic the best model was I-QOL Social Embarrassment Score modelled linearly only. Best fit results were better in the idiopathic (n=2351: MAE = 0.10. RMSE = 0.14) than neurogenic sample (n=254: MAE = 0.17. RMSE = 0.22). **CONCLUSIONS:** This research provides algorithms for mapping EQ-5D index scores from I-QOL allowing calculation of appropriate preference-based health-related quality-of-life scores for use in cost-effectiveness analyses when only I-QOL data are available. The strongest results were for idiopathic patients, but those for neurogenic are consistent with other published mapping studies.

MA2

MAPPING FACT-P TO COUNTRY SPECIFIC PATIENT HEALTH STATUS MEASURED BY EQ-5D IN METASTATIC CASTRATE RESISTANT PROSTATE CANCER PATIENTS

Spencer M[1], Diels J[2]
[1]Janssen-Cilag UK Limited, High Wycombe, UK, [2]Janssen Pharmaceutica, Beerse, Belgium

OBJECTIVES: To construct and validate a prediction model of preference-adjusted health status (EQ-5D) for metastatic castrate resistant prostate cancer (CRPC) patients using FACT-P (Functional Assessment of Cancer Therapy–Prostate), a multidimensional prostate cancer-specific health-related quality of life instrument. **METHODS:** Patient-level data were obtained for CRPC patients from the Adelphi Group Prostate Cancer Disease Specific Program (DSP) data, a multinational cross-sectional study of prostate cancer patients conducted in France, Germany, Italy, Spain and UK during 2009 to 2010. EQ-5D and FACT-P were available for a subset of patients. Country specific utility values were derived from EQ-5D profiles based on value sets available for 8 countries and the EU. Predictive validity of the FACT-P subscales and patient demographics for utility was tested using ordinary least square (OLS), median, Gamma and Tobit multivariate regression models, and predictive algorithms developed to convert FACT-P to EQ-5D utilities for different value sets. **RESULTS:** Values for both FACT-P (mean=85.4) and EQ-5D were available for 291 patients (mean age =70.7). A total of 57% of patients were treated with chemotherapy at the time of assessment, 10% had prior chemotherapy, and 33% were chemotherapy naive. Mean estimated country-specific utilities varied between 0.59 (New Zealand) and 0.76 (Germany). OLS and TOBIT regression were the best-performing models, explaining between 34.6% (Danish) and 46.8% (EU) of the observed EQ-5D variation. The physical and functional well-being subscales had the highest explanatory value. The social well-being and prostate cancer specific subscales, and patient age and BMI did not have statistically significant additional explanatory value. **CONCLUSIONS:** The developed algorithms enable to translate cancer-specific health-related quality of life measures to preference-adjusted health status in metastatic CRPC patients, taking into account local country-specific utility weights. The findings will help to develop health status adjustments in cost-utility analyses used in appraising health care technologies.

MA3

MAPPING THE DIABETES HEALTH PROFILE (DHP-18) ONTO THE EQ-5D AND SF-6D GENERIC PREFERENCE BASED MEASURES OF HEALTH

Meadows K[1], Mulhern B[2], Rowen D[3], Brazier J[2]
[1]DHP Research & Consultancy Ltd, London, UK, [2]University of Sheffield, Sheffield, UK, [3]University of Sheffield, Sheffield, South Yorkshire, UK

OBJECTIVES: To carry out cost utility analysis, utility values can be derived using generic preference based measures such as EQ-5D or SF-6D. In some settings generic measures are not used, and mapping functions are being developed to predict utility scores from condition specific measures. The aim of this study is to map the DHP-18 - a diabetes-specific HRQoL patient reported outcome measure - onto EQ-5D and SF-6D utility scores for type 1 and type 2 diabetes mellitus populations. **METHODS:** The data used was pooled from a longitudinal study of quality of life in diabetes. OLS, GLS and Tobit models regressing DHP dimensions and, separately, DHP items onto EQ-5D and SF-6D index scores for both type 1 (n=236) and type 2 (n=2358) diabetes populations were applied. **RESULTS:** For both the EQ-5D and SF-6D, the GLS model mapping selected DHP-18 item scores, squared item scores, age and gender onto the utility index provided the best fit, and this was the case for both the type 1 and type 2 populations (R2 EQ-5D type 1: 0.516; EQ-5D type 2: 0.290; SF-6D type 1: 0.647; SF-6D type 2: 0.396). The models under predict utility when the state is severe and over predict when the state is mild. The error associated with the models was lower for SF-6D than for EQ-5D due to differences in the range of the measures. **CONCLUSIONS:** The DHP-18 items can predict both the EQ-5D and SF-6D utility scores with acceptable precision with the mapping algorithm for the SF-6D displaying a higher level of precision. The mapping functions developed from the models can be used to predict utility scores in settings where the EQ-5D or SF-6D have not been used alongside the DHP-18. However mapping should be considered second best in comparison to using generic measures in research studies.

MA4

MODELLING EQ-5D HEALTH STATE VALUES: DEVELOPING A LIMITED DEPENDENT VARIABLE, MIXTURE MODELING APPROACH

Wailoo AJ, Hernández M, Ara R
University of Sheffield, Sheffield, UK

OBJECTIVES: We have previously developed an adjusted, limited dependent variable, mixture model (ALDMM) approach for estimating EQ-5D utility values from a range of covariates which reflects the upper bound, skewness and gaps in the distribution of EQ-5D. The three class ALDMM has been demonstrated to perform better than standard approaches on aggregate in a rheumatoid arthritis (RA) dataset but was not superior at very poor health states. Here we refine the method and apply it to a much larger RA dataset. **METHODS:** Using an observational dataset of RA patients (n=16,000) we estimate EQ-5D utility values (UK tariff) as a function of Health Assessment Questionnaire (HAQ), pain, age and sex. This was done using linear, Tobit, three and four class ALDMMs. We further adjusted the ALDMM to account for the lower EQ-5D bound. **RESULTS:** EQ-5D is estimated as a function of HAQ, pain and pain2 as well as age and sex. Previous results were replicated at extremely poor health states in this very large dataset. By including the additional adjustment for very poor health states, the ALDMM outperforms all others tested in terms of model fit and appropriateness of the predictions across the entire range of EQ-5D **CONCLUSIONS:** The ALDMM approach is designed to appropriately reflect the range of challenges that arise from the EQ-5D distribution. Standard models are not as appropriate and fit the data less well. It may be that an additional adjustment to the ALDMM is required to model extremely serious health states, which are often of critical importance in cost effectiveness models, though the relative scarcity and credibility of data at this extreme remain a concern.

PODIUM SESSION III: LOOKING BEYOND EXISTING HORIZONS

MO1

METHODS FOR EXTRAPOLATING SURVIVAL DATA USED IN NICE TECHNOLOGY APPRAISALS: INCONSISTENCIES AND LIMITATIONS

Latimer N
University of Sheffield, Sheffield, South Yorkshire, UK

OBJECTIVES: Treatments that impact upon survival form a high proportion of the interventions appraised by the National Institute for Health and Clinical Excellence (NICE). Survival data are commonly censored and therefore extrapolation is required to estimate the full impact of the new intervention. There are a range of approaches for conducting survival analysis in these circumstances, and these can lead to widely varying survival estimates and incremental cost-effectiveness ratios (ICERs). We reviewed a subset of NICE Technology Appraisals (TAs) to identify and analyse methods that are commonly used in practice. **METHODS:** We identified all completed NICE TAs that appraised new treatments for advanced and/or metastatic cancer and analysed methods for estimating survival and justifications for the chosen approach. **RESULTS:** By December 2009 NICE had completed 45 TAs that focussed on advanced and/or metastatic cancer. Parametric models were used in 71% of these. Weibull and exponential models were most commonly used (in 51% and 44% of the reviewed TAs, respectively), with Gompertz, log-logistic, log normal and gamma models used infrequently. Piecewise parametric models and other more flexible methods were seldom used. Justifications of chosen approaches were not systematic and were usually overly simplistic. **CONCLUSIONS:** Survival analysis methods differ significantly across NICE TAs. This is expected because different methods are appropriate in different circumstances. However, the majority of TAs did not take a systematic approach to survival analysis and did not fully justify chosen methods. Therefore inappropriate methods may have been used. Different models can lead to large variations in ICERs – for example in NICE TA178 log-logistic models led to an ICER of £40,000, compared to £75,000 when Gompertz models were used. Hence it is clearly of great importance to select appropriate models. This review has contributed to a NICE Technical Support Document on extrapolation with patient-level data.

MO2

EXTRAPOLATION IN ONCOLOGY MODELLING: NOVEL METHODS FOR NOVEL COMPOUNDS

Annemans L[1], Asukai Y[2], Barzey V[2], Kotapati S[3], Lees M[4], Van Baardewijk M[5], Wang Q[4], Batty AJ[6], Fisher D[6]
[1]Ghent University, Ghent, Belgium, [2]IMS Health, London, UK, [3]Bristol-Myers Squibb Pharmaceuticals, Wallingford, CT, USA, [4]Bristol-Myers Squibb, Uxbridge, Middlesex, UK, [5]Bristol-Myers Squibb, Braine L'Alleud, Belgium, [6]BresMed Health Solutions, Sheffield, South Yorkshire, UK

OBJECTIVES: Immunotherapies such as ipilimumab and IL-2 show delayed but durable response leading to stabilization of symptoms and extended OS after an initial drop-off in the KM curve. Our objective was to review and challenge currently available economic modelling methods when applied to such emerging therapies with new mechanisms of action (MoA). **METHODS:** As alternatives to stan-

dard OS extrapolation methods which fit 'traditional' parametric survival distributions to patient-level data, two different methods were explored in the modelling of OS beyond the trial duration (55 months) for the novel immunotherapy ipilimumab. In the first approach, the hazard rate from the Kaplan-Meier (KM) curve between 24 and 36 months (before reaching a plateau) was used to extend the curve. In the second approach, different parametric curves were fitted to the period of 18 months onwards. Akaike's Information Criterion (AIC) was used to determine the best fit curve. **RESULTS:** When compared to standard OS extrapolation methods, both methods exhibited a better visual fit to the data. Both approaches allow the hazard of the extrapolated tail to be based on a section of the KM curve that is more appropriate in describing the long-term survival of these patients. The hazard rate approach does not allow for a formal comparison with AIC, but allows extrapolation in line with the clinical interpretation. The 'parametric curves' approach allows for a statistically better fit with the patient level data using conventional AIC criteria. Both methods are in line with long-term observations of immunotherapy. **CONCLUSION:** For novel cancer therapies whose KM curves are not well described by standard survival distributions, other methods of extrapolation should be explored in conjunction with an understanding of the clinical rationale. In this case study, two alternatives are presented that describe the OS of immunotherapy patients in a more suitable way.

MO3
A METHODOLOGICAL FRAMEWORK FOR DEVELOPING MODELS OF WHOLE DISEASE AREAS TO INFORM RESOURCE ALLOCATION DECISIONS

Tappenden P, Brennan A, Chilcott J, Squires H
University of Sheffield, Sheffield, South Yorkshire, UK

OBJECTIVES: Conventional economic evaluation involves piecewise comparisons of competing interventions at a single point in a broader care pathway. **METHODS:** This approach is subject to several problems: a) there remains an ongoing debate surrounding the appropriateness of threshold-based decision rules and whether their repeated use will maximise health; b) restricting the model scope to a single decision point means that other adoption decisions elsewhere in the disease pathway may be treated as independent of the problem under consideration; and c) the absence of model development guidance leads to inconsistencies between analyses addressing similar decision problems. In light of these problems, this study puts forward the notion of "Whole Disease Modelling." This involves simulating whole disease and treatment pathways within a single model, from preclinical disease through to diagnosis and referral, adjuvant treatment, follow-up, potential recurrence, palliative treatment, end-of-life care and eventual death. A methodological framework has been developed based on three key principles: 1) the model boundary and breadth should capture all relevant aspects of the disease and its treatment; 2) the model should be developed such that the decision node is conceptually transferable across the pathway; and 3) the costs and consequences of service elements should be structurally related. **RESULTS:** Case study applications in colorectal cancer services suggest that Whole Disease Modelling is feasible and may provide a consistent platform for economic analysis at virtually any point in a disease pathway using multiple economic decision rules. **CONCLUSIONS:** The value of the approach may be realised when: multiple decision problems require formal economic analysis at a single timepoint; services are subject to rapid innovation and the model can be re-used; a substantial proportion of currently provided service elements have not previously been subjected to economic analysis, and; standard cost-utility decision rules fail to reflect the complexity of the decision-makers' objectives.

MO4
OUTCOMES BEYOND HEALTH

Joore MA[1], Dellaert B[2], Spijkers L[1], Severens JL[3], Krabbe P[4], Dirksen C[5]
[1]*MUMC, Maastricht, The Netherlands,* [2]*EUR, Rotterdam, The Netherlands,* [3]*Erasmus University Rotterdam, Rotterdam, The Netherlands,* [4]*RUG, Groningen, The Netherlands,* [5]*MUMC, maastricht, The Netherlands*

OBJECTIVES: The aim of this study was to investigate whether broadening the evaluative space in an economic evaluation would lead to other outcomes, and hence policy recommendations. **METHODS:** Two discrete choice experiments (DCE) were conducted in a population of patients who had been treated for varicose vein disease (N=390) either by foam sclerotherapy or surgical stripping. In the Health DCE the treatments were described in terms of health outcomes attributes only (based on the EQ5D dimensions). In the Extended DCE the treatments were described in terms of the same health outcomes attributes and other aspects (Waiting time, Probability of retreatment and Nature of treatment). The differences in the levels were collected in a clinical trial and entered into the preference models to calculate the differnce in utility between those treatments. The ΔU in both models was standardised on a [-1,1] scale. The incremental costs of foamsclerotherapy versus surgical stripping, as observed in the clinical trial, amounted to -€1123. **RESULTS:** All attributes were statistically significant, except for Waiting time and Probability of retreatment. The relative importances and the ranks of the health attributes differed between the models. The patients preferred surgical treatment if only health outcomes were considered, while the patients preferred dermatological treatment if also aspects beyond health outcomes were considered in the choice: ΔUhealth=-0.0109; ΔUextended=0.3971. When incremental utility was based on health outcomes only alone, the incremental cost-utility ratio was €103,027. When incremental utility was based broader outcomes, the incremental utility ratio indicated dominance. **CONCLUSIONS:** The results suggest that recommendation for policy would changed if not only health outcomes but also broader outcomes are considered. The results confirm that a restriction to health outcomes in the (economic) evaluation of health care leads to the maximization of health, but not necessarily to the maximization of benefit in a broader sense.

PODIUM SESSION III:
FLOATING THRESHOLDS AND BY PASSES: RISK SHARING AND PATIENT ACCESS

RS1
LITERATURE REVIEW ON PATIENT ACCESS SCHEMES, FLEXIBLE PRICING SCHEMES AND RISK SHARING AGREEMENTS FOR MEDICINES

Puig-Peiró R, Mestre-Ferrandiz J, Sussex J, Towse A
Office of Health Economics, London, UK

OBJECTIVES: To identify existing knowledge about the costs and benefits, assessed either quantitatively or qualitatively, of performance based reimbursement, risk sharing schemes, patient access schemes, and flexible pricing schemes for pharmaceuticals. **METHODS:** A systematic literature review was conducted using PubMed for the period January 2008 - April 2011. The terms "risk sharing", "flexible pricing", "patient access schemes", and "performance-based reimbursement" were searched in titles and abstracts. **RESULTS:** The search provided 62 records and after screening the number was reduced to 31. After full assessments of these studies, a total of 24 formed the basis of the review. More than 40 per cent of the publications referred to the Multiple Sclerosis Risk Sharing Scheme implemented in the UK since 2002. The review did not identify any cost benefit analysis evaluating the overall economic impact of schemes in monetary terms. All studies discussed costs and benefits qualitatively and in some cases, when known, some costs were reported. Schemes' key stakeholders – health service employees, companies, regulators –bear different costs and benefits and conflicting incentives may arise. Costs and benefits widely vary depending on the characteristics of the scheme. **CONCLUSIONS:** There is lack of consensus on the welfare consequences of the schemes and their social desirability. Identified benefits are countered by significant costs and the overall balance remains unclear. Further research is necessary: a) to assess in a transparent way to what extent the transactional costs and administrative burden are shared between payers and pharmaceutical companies, as they constitute an important barrier for the implementation of the schemes, and b) to aid design of a successful Value Based Pricing system for new medicines in the UK, given the similar principles that underpin outcome-based schemes where prices are set to match "real world" NHS value in practice.

RS2
COST-EFFECTIVENESS OF END-OF-LIFE, LIFE-EXTENDING INTERVENTIONS: NICE'S COST-EFFECTIVENESS THRESHOLD EXPLORED

Hamerslag L, Haynes S, Kusel J, Costello S
Costello Medical Consulting Ltd, Cambridge, UK

OBJECTIVES: It is widely recognised that the National Institute for Health and Clinical Excellence (NICE) in the UK employs cost-effectiveness thresholds in health technology appraisal decision-making. This incremental cost-effectiveness ratio (ICER) threshold has been topic of much debate and is estimated to lie around £30,000 per quality-adjusted life-year (QALY) gained. In December 2008, NICE approved supplementary advice to reconsider this threshold for life-extending, end-of-life interventions. This policy applies to treatments indicated for small patient populations with life expectancies of usually under 24 months, that typically prolong survival by at least 3 months. The aim of this study was to explore NICE's increased ICER threshold when end-of-life conditions are taken into account. **METHODS:** All NICE technology appraisals issued between December 2008 and June 2011 were reviewed. The appraisals in which end-of-life considerations applied were identified and ICERs from these appraisals were extracted. **RESULTS:** In total, 53 single technology appraisals were published in the timeframe considered; of these, only 13 fulfilled the end-of-life criteria, all concerning treatments for cancer. The final ICERs of these 13 interventions ranged from £31,800 to £68,000, although 10 out of 13 manufacturers employed patient access schemes to lower these values. Both the highest ICER that was approved and the lowest ICER that was not approved were £49,300 per QALY gained. Interestingly, both of these appraisals concerned interventions for the treatment of advanced renal cell carcinoma, implying that other factors must have been taken into account by NICE to reach this judgement. **CONCLUSIONS:** Cost-effectiveness seems to be the most important criterion for NICE in their health technology appraisals. For end-of-life, life-extending treatments, the cost-effectiveness threshold appears to lie around £50,000 per QALY. However, review of individual appraisals shows that other factors such as uncertainty in the estimates and unmet need are also taken into account in NICE's decision-making.

RS3
EVIDENCE, PROCESS OR CONTEXT? EXAMINING THE FACTORS THAT DRIVE COVERAGE DECISIONS OF PHARMACEUTICALS BY HEALTH TECHNOLOGY ASSESSMENT BODIES IN EUROPE

Cerri K, Fernández JL, Knapp M
London School of Economics and Political Science, London , UK

OBJECTIVES: In Europe, Health Technology Assessment (HTA) bodies produce coverage decisions that guide public funding of pharmaceuticals. This analysis examines and weights those factors that drive HTA coverage decisions, focusing on the National Institute for Health and Clinical Excellence (NICE) in England and Wales, the Scottish Medicines Consortium (SMC), the Dutch College voor Zorgverzekeringen (CVZ), and the French Haute Autorité de Sante (HAS). **METHODS:** A dataset of approximately 1000 HTA coverage decisions by NICE, SMC, CVZ and HAS from the period 2004-2009 was created, containing more than 30 clinical, economic, process and socio-economic factors extracted from published HTA reports. A three-cate-